

DEFECTIVE DEVELOPMENT AND DISEASE, WITH
SPECIAL REFERENCE TO THE CURABILITY
OF CONSUMPTION AND CANCER.

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The problems about to be discussed are of interest to microscopists, although in one sense more strictly adapted to another audience. It would have been desirable to have given more detailed observations in reference to histological, biological, and other points involved, instead of dwelling so largely upon the general aspects of the subject. Nevertheless, the paper may be, I hope, of some service to the working microscopist as indicating lines of research that it is specially desirable to follow.

Our knowledge of the agency of bacteria in the production of disease has advanced so rapidly since the pioneer discovery of the bacillus of tuberculosis in 1883 that there is danger of forgetting that there is another side to the question, having reference to the perfection of organization of the human frame, and its consequent resisting power to disease. Indeed, there are disease conditions due to defective development solely, in the entire absence of bacterial infection of any sort. Thus the degenerative changes due to old age result in enfeeblement amounting to positive disease, and yet there is no microbe of old age, at least not any thus far discovered. Nor is there any microbe of nearsightedness, nor of squint, nor of harelip, nor of lack of brain and nerve, nor of any of the thousand and one imperfections and peculiarities, many of them racial, like flat noses and thick lips, that appear in those having otherwise fine physique.

Really the human body is no better than patch-work, loosely put together and weak at many points. Malformations about the neck, commonly spoken of as scrofulous, may signify noth-

ing more than imperfect closure of the embryonic bronchial fissures in that location. The tibia and fibula being of nearly equal size, and the ankles crooked in the embryo, undue persistence of these forms may originate coarse ankles and clumsy gait, presenting the appearance of positive disease, whereas it is a purely developmental defect. So, too, the appendix vermiformis, that supernumerary tattered end of the patch-work of the body, appears to serve no purpose except to catch dirt and infection, and destroy life on absurdly small provocation, gratifying the disciples of Malthus, but no one else. In like manner the wisdom tooth is a superfluity, except so far as the dentist is concerned, and there are many other abnormalities of like character pleasing to no one, unless it be the student of teratology, and the surgeon.

In the subject chosen for this paper, cancer and consumption are specially named in connection with defective development, as representing two aspects of the entire question, and at the same time as being essentially most important because of their serious nature. With our present knowledge, cancer represents all that is worst among diseases not due to specific micro-organisms, and consumption all that is worst among diseases produced by such organisms.

Until inoculation experiments have demonstrated that cancer is contagious, its bacterial origin cannot be assumed. Cancer appears to be most closely allied to eczema, the chief difference being that it affects epithelial cells other than those chiefly involved in eczema. Cancer, like eczema, may be produced by many sorts of irritation, bacterial or otherwise, there being no specific parasitic organism in either disease, and both alike being non-contagious. Thus, tobacco-smokers' cancer starts from the irritation of the lip by the pipe, at the outset resembling the eczema to which it is so closely allied, and which is associated also with cancer of the breast, as was pointed out by Sir James Paget. The difference in the behaviour of cancer and eczema in respect to danger to life is, according to this view, due to the fact that in the former the epithelial cells involved have a power of growth resembling that of various appendages of the skin,

such as the hair and nails, but not safeguarded in the same way. Cancer cannot be cast off as the horse sheds his coat, or the stag his antlers, or the snake its skin, nor can it be kept trimmed, like the hair and nails, although something of this sort is often attempted surgically.

Thus cancer may be taken as the type of all that is worst in the diseases due to faulty growth. It does not stop with the formation of tissues of low vitality, and specially vulnerable to the forms of infection capable of producing ulceration, but goes right on increasing in bulk, producing injurious pressure effects on surrounding parts and destroying their vitality. The products of the perverted cell activity in cancer, like many other wastes of the body, appear to be poisonous when retained, not resembling, except in appearance, the corresponding exudation in eczema, which is harmless. Thus the epithelial origin and type of growth of cancer is the most serious phase of the question as to the nature and consequences of defect of development affecting the cellular structure of parts of the body.

Consumption, on the other hand, is the type of all that is worst in the class of diseases that are plainly due to specific forms of bacterial infection. Unlike the bacilli of many other infectious diseases, that producing consumption is not destroyed by the products of its own activity. Hence the futility of the search for an anti-toxin for this disease derived from its bacillus, and hence also its tendency to progress to a fatal termination. Self limited diseases only are likely to be controlled to any important extent by the methods of serum treatment thus far devised.

Thus broadly these are two types of disease, the one primarily due to defect of development, and the other to specific bacterial infection. The former produces abnormal growth, which may be harmless, like a wart, or malignant, like cancer; the latter produces the congeries of symptoms comprised under the general term inflammation.

The former of these classes of diseases may exist independently of the latter. There may be hereditary or congenital tissue conditions originating idiocy, epilepsy, deafmuteism,

dwarfishness, malformations, and the like, without bacterial infection of any sort. It is a question, however, whether bacterial diseases can gain a foothold, on the other hand, except at some point where there is lowered resisting power, through defect of development. As a matter of fact a very large proportion of the infectious diseases attack primarily portions of the body exhibiting deficiencies in respect to function or structure, or both. It is of fundamental importance to inquire in what way and to what extent imperfections of development are associated with diseases of every kind, excluding none, bacterial or otherwise. Hence the propriety of discussing both consumption and cancer in this connection.

The identification of the markings indicating persistence of rudimentary and embryonic forms is the first step towards a proper understanding of the questions of cellular pathology involved. Such identification is not difficult in a large proportion of cases. Thus the tonsils are rudimentary structures, tending to disappear as adult life approaches, and having little if any function at any time, and consequently having small resisting power, are the usual starting point of disease in the throat. In like manner in the mouth the wisdom tooth is well nigh functionless and specially subject to decay. In the chest the thymus gland reaches its maximum size at the age of two years, and nearly disappears at the age of twenty, and has very little apparent function. This being the fact its agency in the production of disease is worthy of far more careful scrutiny than it has thus far received. In a few instances this gland has been found to be inflamed and swollen where children have died suddenly and unexpectedly without any other conspicuous symptom than some difficulty of breathing. Like the appendix vermiformis, another of these troublesome rudimentary structures, until recently thought to be quite inoffensive, the thymus gland may play a much more important part as a cause of death than has heretofore been supposed. Thus also cretinism is a form of stunted and irregular growth due, apparently, not to bacterial infection, but to imperfection of the

thyroid gland as shown by the improvement that results from thyroid feeding in these cases.

Embryonic and rudimentary markings in general are closely related to disease processes. In a case observed by the writer cancer dissected out accurately the surfaces which form the upper bronchial cleft in the embryo, and whose imperfect closure produces harelip and cleft-palate. Erysipelas has been observed to follow the line of these clefts also. In like manner decay in the teeth and bones follows epiphyseal and other lines connected with processes of development. In each case of this sort the spread of disease appears to have had reference to lowered resisting power of the tissues rather than to distribution of blood supply, or to lymphatic channels, or any other like agency.

So too in the case of organs and parts of the body that fail of their normal development there is increased susceptibility to disease. The eye that is congenitally imperfect is specially subject to inflammation. The ear that does not hear well through malformation is most readily attacked by disease. Incomplete closure of the opening that exists normally previous to birth, between the two sides of the heart, entails increased liability to serious consequences from disease, an ordinary cold, it may be, proving fatal in such children. Failure of development of parts of the nervous system may disturb mentality, nutrition, muscular action, and the like. Thus there is not an organ or part of the body that may not exhibit deficiency and consequent disease.

Embryology, especially, throws a flood of light on questions such as these, and becomes an exceedingly fascinating study, as a department of microscopical research. In other words it is not altogether a question of bacteriology, but of the study of the tissues at various stages of their growth and in their various relations. Indeed in the case of cancer this may prove to be the only means of solving the problem of its causation. If it is not due to any specific micro-organism, there is no other resource than to institute a careful search for rudimentary, functionless or disappearing organs or structures in the

tissues that are found to be specially subject to cancerous disease. In this connection it is of special interest to note that cancer, unlike infectious diseases, is most apt to occur late in life, pointing to degenerative changes rather than bacterial invasion as its cause.

Still, if cancer should be found to be due to a parasite of any sort it would be none the less important to determine the conditions of lowered resistance which enable it to gain a foothold in the manner indicated throughout the course of the present discussion.

We have at Buffalo, N. Y., a State Laboratory specially devoted to research in regard to cancer. This is a step in the right direction, and it would seem that similar original research in regard to a multitude of questions concerning consumption would accomplish more than such ordinary State Sanitaria for consumptives as have been proposed. It has seemed to the writer, also, that improved methods of recording cases might be of great service in many state institutions.

For years the writer has made it a practice to identify and note, as far as possible, all the markings, even the most insignificant, indicating defective development. Not unfrequently the results are exceedingly interesting, especially when such stigmata are numerous though not conspicuous. For example, a person met casually was seen to have a slight cleft in the iris just below the pupil of the eye. The bridge of the nose was hollowed and of the infantile type. The bony bridge across the lower part of the outlet of the nostril was lacking, the upper lip sinking in at that point. There was evidence of a tendency to harelip in the center of the lower lip, which is rather uncommon, the upper lip being the ordinary location of such malformation. The upper jaw was imperfectly developed, being small in comparison with the lower jaw. The teeth were irregular, and the skin and hair coarse. Darwin's tubercle was specially well marked on the inner margin of the rim of the ear. The neck was thick and of the type sometimes called scrofulous. These and other markings, many of which caricaturists seize upon and exaggerate habitually, would give even

the most casual observer the impression that the individual in question was of a low order of development, both physically and mentally. As a matter of fact he was an epileptic, and a criminal, and has since died of consumption.

The disease history in any such case, taken in connection with the record of such markings, becomes very instructive. By such means it may become possible to identify much more perfectly than has been the rule heretofore, the precise defects of development which give access to each particular form of disease, thus affording a basis for more accurate histological study.

Indeed, almost every form of disease, as well as cancer and consumption, exhibits a marked predilection for particular organs and parts of the body. Much light will be thrown upon such selective affinity of disease by studying the relation of the parts involved to embryonic forms and to homologous structures and tissues in animals, and especially to the markings indicating defective development. This is the office of comparative pathology, which bids fair to become a very progressive department of medical science in the near future.

It is possible that the time may come in the course of such investigations as have been outlined when early and complete removal of the part affected will not be our only resource in dealing with cancer. It is not likely that an anti-toxin will be found for cancer, it, like consumption, not being a self-limited disease. Still the writer has seen a cancerous ulcer heal as the result of its becoming the seat of an attack of erysipelas, but the relief was only temporary, the ulceration recurring in about a year and finally causing death. From some microscopic observations that were made in connection with this case it was inferred that the cancer itself was not affected favorably or otherwise by the erysipelas, the real effect that produced the apparent improvement being nothing more than the healing of a subsidiary ulceration due to some form of infection that had fastened itself on the cancerous area. In other words, the erysipelas in this case acted on the principle of an anti-streptococcus

serum so far as the ulceration was concerned, but did not really benefit the cancer itself.

So far as the prophylaxis of cancer is concerned, we can only recommend the avoidance of sources of irritation, like the smoker's pipe in tobacco cancer. Peculiarities in regard to the geographical distribution of the disease that are just beginning to attract attention may afford a clue to racial and other hereditary influences on which it may depend. The effect of environment on developmental conditions is very decided, and may play a part in preventing or accelerating the spread of cancer. These questions are very large and difficult, and their complete solution will require extended research along the lines that have been sketched with a free hand in the course of this paper.

Consumption, on the other hand, belongs in the class of bacterial diseases with reference to which the case is much simpler. Still it has its developmental relations, having a marked predilection for particular lung and bony tissue. It is probable that lowered resisting power in these parts of the body is necessary in order that it may gain a foothold. Thus predisposition on the part of the tissues is requisite, as well as presence of infection, as has been indicated throughout the course of the discussion. The bacillus does not pass from parent to child by heredity, but only special vulnerability of the tissues in which it gains a lodgement. Thus whatever tends to secure perfect development, and fortify resisting power, will aid in the prevention and cure of consumption also.

But this is not our only resource. Consumption is a perfectly curable disease in a large proportion of cases, because of certain peculiarities of the bacillus on which it depends. This is the fact in the earlier stages of the disease more particularly. As has already been intimated, there is no anti-toxic serum that is likely to be effectual against it. Nevertheless, consumption is curable in a very simple way, which as soon as it is mentioned, will seem so very obvious that it will be understood and corroborated by experiences within the range of observation of almost any one. And yet this is practically the first public

announcement of the result of studies leading definitely to this conclusion.

The point is that the bacillus of tuberculosis thrives only at a temperature closely approximating that of the human body. At a lower temperature, especially, its growth is retarded to such an extent that it may become dormant and in this condition be destroyed by the processes akin to digestion that are going on constantly in the air passages and lungs. Or, at a later stage, if it have invaded the tissues more deeply, it may be destroyed by the leucocytes and other vital agents whose office it is to enable the human frame to resist the invasion of disease.

That it is possible to lower the temperature of the lungs to a considerable degree by the inhalation of air such as is met with in ordinary outdoor living may be shown by a simple experiment. It is possible to arrange a thermometer in a tube, and so regulate the breathing as to obtain very nearly the temperature of the air exhaled. If this be done in air at the ordinary temperature of a room it will be found that the air that has passed through the lung does not quite reach the temperature of the body, but comes very near it if the room be very warm. If then the experiment be tried outdoors in much colder air it will be found that the air exhaled may fall short as much as fifteen or twenty degrees of reaching the temperature of the body. If the bacillus is anywhere in contact with air so cold as this its growth must certainly be greatly retarded and there is very good evidence that this is the fact in the lung. It is probable that the bacillus is located very superficially in the mucous lining of the air passages for a long time, it may be for weeks and months after infection, acting like foreign matter such as dust in this location, until growth begins and the tissues are invaded superficially at the outset but more deeply later. If at this stage the individual infected houses himself up in a warm room constantly, because of the slight hacking cough, as is very apt to happen, the infection gains a firmer foothold, and the chances of recovery diminish steadily. Hence the desirability of outdoor life for consumptives, and plenty of fresh cold air at night. Hence also the advantage of

residence at a considerable altitude, the dry air taking up heat more readily, and its rarefied condition quickening and deepening respiration, so that the air cells are more fully expanded and more deeply penetrated. Hence also the comparative immunity from consumption and other lung troubles in the Arctic regions, although this has been ascribed to cod-liver oil, which fails of any such effect in lower latitudes, it being the crisp cold that really does the good. It is the explanation of such benefit as is derived without clear understanding of the reasons, perhaps from living on a ranch, or going to some distant sanitarium, or taking a sea voyage, in all which cases some measure of outdoor life is insisted on. Even within the tropics outdoor life, night and day, may prove effectual on the principle that has been stated.

In order to secure the greatest benefit the vital forces should be strengthened by plentiful and nutritious diet, forced feeding in fact. The change to habitual outdoor life and sleeping in a cool room should be made so gradually and with such precautions as will obviate lowered resisting power through shock to the nervous system.

Many instances are known to the writer in which there has been recovery from consumption affecting the lungs, and instances likewise in which there was failure because the disease was situated in the bones or elsewhere, in such manner as not to be accessible to the benefit from open-air life that has been described.

In this connection it is of very great interest to note that cattle are specially susceptible to infection by the bacillus of tuberculosis, but that it does not affect the lungs in their case so frequently as in the human species, the reasons for which will appear in the further course of the discussion, it depending in part, perhaps, upon the manner of their infection, and in part upon their manner of living.

Normally the temperature of the ox is somewhat higher than that of man, so that cattle are more readily infected for this reason. But growth of the bacillus in the lung would be retarded by their outdoor life at certain seasons, so that as a rule

they succumb to tubercular disease scattered in other parts of the body. Horses, on the other hand, are immune, their temperature normally being somewhat below that of man, and their lungs fully and freely expanded in the open air at frequent intervals, instead of being almost entirely disused as in the case of cattle confined to their stalls for weeks and months together, and at best only walking slowly about in the open air. As a matter of fact, cattle that run wild on the plains are as free from tuberculosis as horses. Lecturers at dairymen's conventions, who tell the farmers that they must keep their cattle warm if they would secure record yields of milk and butter, are responsible for much of the spread of tuberculosis.

But perhaps the greatest danger of all is from the common barn-door fowl. The prevalence of tuberculosis among graminivorous birds, whose temperature is normally 105° , is very significant from the point of view of the present discussion. Their flesh is not eaten raw, nor do they yield milk, so that there is no great danger to the human species from tuberculosis in fowls, but their droppings falling into the hay and grain become a source of great danger to cattle especially, whose intestinal tract is most liable to infection from this source. Indeed, this may be the explanation of the reinfection of herds on farms where they have been slaughtered, wholly or in part, in response to the tuberculin test.

The idea of controlling the activity of disease-producing bacilli by temperature changes has other applications already in use that are corroborative of the position here taken. Thus the treatment of typhoid fever by cold baths, or by the application of cold to the abdomen, is in successful use. In like manner the application of cold to the chest has been employed in pneumonia. So, too, the warmth of a poultice may hinder the activity of certain bacilli by raising the temperature beyond the point at which they are best able to grow.

In short, the principle is that employed by Pasteur at the very outset of his studies which originated the modern science of bacteriology, when he hit upon the idea of employing cold to prevent fermentation in beer. He likewise made the dis-

covery that the bacillus of anthrax, which is fatal to cattle, horses, and sheep, does not propagate at a temperature very much above 100° , and hence birds, whose temperature normally is 105° , are not susceptible to its attack, unless made to stand in cold water long enough to lower their temperature to the proper degree.

Thus, as every working microscopist knows, temperature control plays a part that can be measured with precision in determining the activity of microbes of every sort. It is to be remembered, however, that the bacillus of tuberculosis is not destroyed in a culture outside the body by a degree of cold that proves fatal in the lungs. It is the resisting power of the body that destroys and eliminates the germ, benumbed and weakened by lowering the temperature. It is to bring out this point clearly that it has been thought best to outline the entire subject of defective development and disease, employing cancer as a typical case in contrast to consumption.

From the point of view of the present discussion it is evident that much of the advice given consumptives in regard to change of climate, outdoor life, and the like, involves some dim idea of the nature of the truth of the matter, but lacks precision, not specifying accurately which are expected to be curative of the measures suggested. With a better understanding in this regard it becomes possible to increase the efficiency of the measures employed, it being known precisely what it is proposed to accomplish. Thus it may become possible to prevent tuberculosis in cattle, as well as in the human species, by proper outdoor exercise of herds and prevention of infection from such sources as fowls.

With these points in view it becomes possible to estimate more accurately the value of various accessory measures, some of which have been hinted at. Experiment has shown that it is possible by forced feeding to determine the sex in bees and tadpoles very readily. It has been claimed recently that this has been accomplished also in the human species. This being the case, it shows what a profound effect nutrition has upon the vital and reproductive organs, and upon heredity. If it is pos-

sible to modify the development of sex by such means, it surely is possible to modify in like manner the resisting power of the body against disease.

As regards heredity, Weissmann in his book on "Germ Plasm" makes it consist in the minute subdivision and transmission from parent to offspring of certain protoplasmic granules. If, however, life be taken away in such manner that the protoplasmic constituents of the body are otherwise undisturbed, the form remains but power is wanting. Brain and nerve force manifest in muscular action, and in the operation of the senses, are requisite for the maintenance of bodily vigor in the individual, and for its transmission to the offspring.

Thus the cure of consumption in the manner that has been described is not a question of cold storage, or life in a cave at a constant temperature, with a view to the absolute freezing out of the germs of such disease. It is rather a question of the full and free exercise of the powers of the body, and their maintenance in such condition that, with some aid from special measures of temperature control, they are able to win a complete victory in a contest that has heretofore been very unequal.

It is to be hoped that observers having the requisite microscopical equipment will be specially alert in regard to the questions that have been raised. It is not a question of lenses altogether, but of knowing what to look for.